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The Tuskegee Legacy Project: history, preliminary scientific findings, and unanticipated societal benefits

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Summary

This article is intended to provide a relatively complete picture of how a pilot study—conceived and initiated within an NIDCR-funded RRCMOH—matured into a solid line of investigation within that center and "with legs"into a fully funded study within the next generation of NIDCR centers on this topic of health disparities, the Centers for Research to Reduce Oral Health Disparities. It highlights the natural opportunity that these centers provide for multicenter, cross-disciplinary research and for research career pipelining for college and dental school students; with a focus, in this case, on minority students.

Furthermore, this series of events demonstrates the rich potential that these types of research centers have to contribute in ways that far exceed the scientific outcomes that form their core. In this instance, the NMOHRC played a central—and critical, if unanticipated—role in contributing to two events of national significance, namely the presidential apology to the African American community for the research abuses of the USPHS–Tuskegee syphilis study and the establishment of the National Center for Bioethics in Research and Health Care at Tuskegee University.

Origins of the Tuskegee Legacy Project

The Tuskegee Legacy Project (TLP) has its origins in casual Web surfing by a biomedical reference librarian on her laptop computer on a fall evening in 1993 while relaxing in the dormer

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Research Centers supported by the NIH are fully intended to create a vortex of scientific activity that goes well beyond the direct scientific aims of the studies initially funded within those centers. The maxim is that the whole should be greater than the sum of its initial constituent studies or parts. We believe that NMOHRC did indeed achieve that maxim—even extending "the whole" to include broad societal impact, well beyond the scope of important, but mere, scientific outcomes—all within the concept and appropriate functions of a scientific NIH-funded research center.

room, which served as the family den. Ms. B.J. Frey, Head Reference Librarian at the University of Connecticut Health Center Biomedical Library, casually mentioned to her husband (R.V.K., one of the authors) that she had just come across a conference announcement that might appeal to him. It was entitled “The Tuskegee Legacy: Doing Bad in the Name of Good” and was described as a 1-day bioethics conference to be held in April 1994 at the University of Virginia, cosponsored by the university's Center for Bioethics and the Historical Collection Section of the campus library.

There were many reasons to attend the conference at the University of Virginia: (1) there was an attractive array of announced academic speakers (bioethicists, medical historians, and medical anthropologists); (2) the keynote presenter was Dr. Jim Jones (author of *Bad Blood*, the definitive history of the United States Public Health Service (USPHS)–Tuskegee Legacy Study); (3) Jim Jones's book, *Bad Blood*, had been a classroom tool of one of the authors of this article (R.V.K.) for several years; (4) the National Institute of Dental and Craniofacial Research (NIDCR) had taken the leadership role at the National Institutes of Health (NIH) on minority health issues by being one of the first NIH institutes to establish a national network of minority health research centers; and (5) the same author (R.V.K.) was director of the Northeastern Minority Oral Health Research Center (NMOHRC), one of four NIDCR-funded Centers for Minority Oral Health (RRCMOH). Due to the above, attendance at the bioethics conference was—of course—“a given,” and plans were rapidly completed.

The imperative was clear: if the NMOHRC—a partnership between the University of Connecticut School of Dental Medicine and the University of Medicine and Dentistry of New Jersey (UMDNJ) that was based in Newark, New Jersey—were to successfully recruit African Americans into its three major studies, issues addressed at this bioethics conference on the “Tuskegee Legacy” might be absolutely necessary to achieving that goal. The three major studies in the NMOHRC were on critical oral health issues that disproportionately affected African Americans in the United States and deserved the best opportunity to yield important health findings on (1) oral manifestations of pediatric AIDS, (2) epidemiologic and genetic risk factors for oral cancer, and (3) changing the behaviors of medically indigent mothers to avoid baby-bottle caries in their children.

The 12-hour Amtrak trip from Hartford, Connecticut to Charlottesville, Virginia for the conference allowed for a complete rereading of *Bad Blood*, to refresh details of that infamous 40-year-long USPHS study, “Untreated Syphilis in the Negro Male.” The 12-hour return train ride 2 days later consisted of reflections on the ideas and facts about the Tuskegee Legacy that were put forth in the presentations during that 1-day meeting. One key thought kept recurring throughout the return train ride. Despite the passion and convictions of all the speakers with regard to the legacy of that USHPS–Tuskegee study (ie, that African Americans were more reluctant to participate in biomedical research because of the abuse they had suffered in that infamous study), this array of highly qualified speakers had achieved the academically impossible. They had collectively talked for over 8 hours and had provided no references on which to base, much less judge, the central hypothesis. Throughout the day, presentation after presentation appeared to assume that the central hypothesis was true; that is, that African Americans were, in fact, more reluctant to participate in biomedical studies and that the USPHS–Tuskegee experiment was at the heart of this reluctance to become a research participant. The presentations focused exclusively on the whys and wherefores of the consequences of this legacy; namely, the difficulty that biomedical research would have in the future in its attempt to conduct scientific studies on minority health issues, given the fact that recruitment of minorities into future studies would be extraordinarily difficult, if not impossible, due to the legacy of USPHS–Tuskegee syphilis study. The legacy of the USPHS–Tuskegee study, however, appeared to be known more in the gut than in the head: everyone felt that it was true, but lacked any quantified research evidence on which to base those feelings.

As we were soon to learn, this was not an isolated instance. One session at a November 1996 symposium at Howard University entitled “Deadly Diseases and People of Color: Are Clinical Trials an Option?” focused on strategies used to improve minority participation in clinical trials and factors that make minorities more reluctant to participate. Like the University of Virginia meeting before it, however, no research data or empirical studies were presented at this symposium, once again pointing to the lack of data and clearly underscoring the need for research on this issue. In February 1997, a conference on “Minority Recruitment in National Cancer Clinical Trials,” sponsored by the Radiation Therapy Oncology Group (RTOG), was held at Tuskegee University to address this topic; that is, the need to review the compliance of the RTOG cancer studies with the NIH guidelines for the inclusion of minorities in research studies. Once again, no experimentally derived, and hence scientifically validated, guidance was provided.

Within days of returning to the activities of the NMOHRC after the bioethics conference at the University of Virginia, and after having conducted a full—but futile—literature search to find those uncited references that would provide evidence in support of the central hypothesis of the Tuskegee Legacy on minority reluctance to serve as research subjects, the course of action was set. A study needed to be designed and conducted within the NMOHRC to demonstrate and quantify this assumed legacy of the USPHS–Tuskegee syphilis study—a must, because all three of the major studies within the NMOHRC required the successful recruitment of African Americans. The study of the Tuskegee Legacy that was initiated became known, appropriately, as the TLP.

The goal of the TLP was to develop an empirical base that would document, directly address, and hopefully mollify the specific concerns harbored by African Americans as they were invited to participate in future studies focused on minority health issues.

Brief background of the USPHS–Tuskegee syphilis study and related issues

The USPHS–Tuskegee syphilis study (1932–1972) is arguably the most infamous biomedical research study in United States history [1]. There is widespread belief that the legacy of this unethical research event is that the African American community has a greater reluctance to participate in clinical research studies as a result of the abuses foisted on the 400 African American sharecroppers in Macon Country, Alabama who were the subjects in this 40-year USPHS study of the effects of untreated syphilis in the African American male. The title of our overall line of investigation—the TLP—was intended to recognize the historical event of the USPHS–Tuskegee syphilis study and to acknowledge that the term Tuskegee Legacy has become a metaphor for the abuse of research subjects in biomedical studies. On May 16, 1997, President Clinton made a public apology from the US government to the survivors of the USPHS–Tuskegee syphilis study and to the African American community as a whole, in which he acknowledged the historical and metaphorical aspects of this issue [2].

Recruitment for participation in biomedical research has always been difficult and complex. Over the past 20 years, only a few empirical studies (usually on highly specific clinical trial subjects) have been carried out that focused on reasons for participation among clinical-trial subjects or reasons for physicians enrolling or failing to enroll subjects. Based on this limited information, advice was then given with regard to recruitment strategies. As scientists have become aware of the need for recruiting diverse samples to ensure that the results of such investigations are generalizable to the range of individuals comprising the United States population, the difficulty and complexity of recruiting subjects has been greatly compounded.

In fact, difficulties in recruitment have been identified as one of the foremost issues facing biomedical clinical researchers today [3,4]. Indeed, major programs funded by the NIH—such as the Women's Health Initiative (estimated to eventually cost in excess of $1 billion) and the

vast majority of AIDS studies—currently face (and will continue to face) this challenge, as new drugs and treatment regimens are developed. Given that much of the health outcome data of interest and relevance resides within the nonparticipating groups, the lack of sufficiently diverse samples will undoubtedly erode the generalizability of the data collected by these and other studies. Recognition of the fact that morbidity, mortality, and at-risk behaviors are socially patterned according to, for example, race/ethnicity, socioeconomic status, age, and gender, was largely responsible for the development of the 1994 NIH guidelines for the inclusion of women and minorities in biomedical studies. Truly successful compliance with these guidelines in biomedical studies will not occur until the recruitment problems are addressed and rectified.

Since the USPHS–Tuskegee study, “Untreated Syphilis in the Negro Male,” ended in disgrace in 1972, it has been widely thought that African Americans are reluctant to participate in biomedical research because of fears of further abuses by researchers [5]. Although a considerable amount has been written about the long-lasting effects of the USPHS–Tuskegee study on the African American community, most of this work has been from a legal, historical, or ethical perspective [6-9]. The term “Tuskegee Legacy,” which originally was used only to describe the events directly resulting from that infamous study, has come to be used as metaphor for the abuse of African Americans within biomedical research [10,11].

Surprisingly, little research has directly examined whether the differential participation of African Americans or other minorities in biomedical studies from that of whites is directly due to the legacy of the USPHS–Tuskegee syphilis study or to other factors. Given that most clinical trials have been carried out among middle-class to upper middle-class white male participants, it is unclear from the limited research available to what extent the lower participation of African Americans and other minority groups is due simply to convenience in subject solicitation by investigators and how much is due to a greater reluctance to participate by minority groups.

The few studies that have focused on Hispanics' participation in biomedical research have noted that lack of information and mistrust of researchers are salient issues for this ethnic group [12]. Another factor that has been identified as limiting Latino recruitment is the actual recruitment location. Recruitment strategies focused on traditional health care settings cannot reach individuals who do not use such services [13,14].

Like other ethnic minority groups, Latinos report more logistical barriers to health care utilization than do other ethnic groups, including transportation problems, lack of child care, insurance, or free time, all of which would likely also limit ability or willingness to participate in research [15-17].

Cultural factors also may affect Latinos' participation in research. Respect for *familismo*, the strong and traditional family values exhibited by most Hispanic Americans [18], is one important factor. Similarly, respect for a powerful father figure who is the family's primary decision maker (*machismo*) may be important when recruiting other family members, for the father's approval may be necessary to elicit others' participation. *Personalismo*, the respect shown during personal interactions, and *simpatia*, the warmth demonstrated during personal interactions, are also important concepts to consider when recruiting participants from these communities, because strategies that do not employ these concepts may be less successful [19,20].

Although the above-described cultural factors clearly have important effects on the research participation of Latinos, a gap in knowledge still persists regarding the possible effects of perceived racism or distrust related to events such as the Tuskegee study on such individuals' research participation.

Nonetheless, investigations of related issues have clearly shown that racism and race-related issues exert significant influence on minority individuals' participation in biomedical research. For example, minority distrust of the medical system was shown by Ballard and colleagues [21] to be a significant deterrent to research participation, and these researchers attributed some of this distrust to minority individuals' perceptions of institutional racism.

Similarly, the clear evidence that African Americans frequently receive lower quality care from the health care system than do whites [22,23] is another factor potentially leading to distrust in the health care system and, in turn, to distrust of health care researchers. For example, although coronary heart disease (CHD) is the leading cause of death for African Americans in the United States [24,25], and cardiac revascularization procedures are well-established treatments for cardiovascular disease [26,27], a smaller proportion of African American patients than white patients receive such procedures in Veterans Administration (VA), Medicare, and other populations [28-33]. Aside from the significant disparities in cardiovascular procedures received, one study found that non-white pneumonia patients received fewer hospital services, with an accompanying longer hospital stay [34] than did white patients. In another study, African American and low-income individuals had higher rates of limb amputation and bilateral orchiectomy, procedures that the authors viewed as reflecting a “less than optimal management of chronic diseases” [22]. Thus, the realities of substandard health care for minority individuals may be a significant barrier to the kind of trust that is necessary for individuals to participate in research studies conducted by the same health care providers and system.

Fear and distrust of the medical care system may also be related to prior experiences of the process of health care received. Many minority individuals may have previously experienced disrespect or clinical mistreatment by health care workers, and thus may be hesitant to expose themselves to additional contact with the system [35-39]. Research in the process of health care has shown that ethnic minority patients receive less empathy, attention, and information from their doctors [40,41]. Such experiences have been hypothesized to relate to greater distrust of the medical care system on the part of African Americans [42] and to result in decreased health care utilization [43]. In related work conducted in the mental health setting, Terrell and colleagues [44-46] have demonstrated that African Americans who had greater distrust in their white counselors were more likely than those who had less distrust to question the provider's credibility and the quality of the care provided, were less satisfied with their care, and were more likely to terminate counseling.

Research on racial differences in health care utilization has clearly demonstrated that African Americans have less access to health care than do their white counterparts [23,32,43,47]. There are wide disparities in the use of particular medical services, even when access is equalized by similar insurance coverage. One recent analysis of Medicare data [22] found that African American and low-income patients were less likely to have ambulatory physician visits, mammograms, and influenza immunizations, but that such individuals were more likely to be hospitalized or to die. Similarly, Escarce and colleagues [23] found that elderly whites were more likely than were elderly African Americans to receive 23 different procedures and tests, with whites receiving more and newer services or those requiring higher technology. Rosenheck, Fontana, and Cottrol [48] found that African American veterans who were provided mental health services from white clinicians received fewer services. Thus, the literature on minority utilization of health care suggests that not only is such health care harder for such individuals to obtain, but that when they obtain it, it is of poorer quality.

Because participation in most clinical trials is facilitated through one's source of health care, access or lack of access to health care is a critical factor to consider when recruiting study participants. Rural and elderly minority populations have least often been included in clinical

trials, possibly for the reasons stated above [39,49]. Conversely, individuals who usually receive health care at tertiary health care facilities are more likely to participate in research [21], because many clinical trials are conducted in these types of facilities. Notably, few trials are conducted at institutions where poor minority patients usually receive health care [50,51]. Further, the extent to which individuals believe that services from tertiary care facilities are accessible (eg, financially, racially/culturally, and in terms of transportation) may determine the use of these facilities [21]. Ballard et al [21] suggested that minority individuals' decreased likelihood of research participation is a function first of racially conscribed socioeconomic factors, which in turn decrease the likelihood of health care utilization, which in turn decreases the likelihood of being offered participation in a clinical study.

Some research has also pointed to racial differences in perceptions of symptoms—that is, the way in which an individual evaluates the severity of a disease and determines whether it is necessary to seek health care or whether the health care being received is appropriate. Symptom perception may thus influence the differential use of health care services for CHD [52,53] and other illnesses. Previous research has shown that African Americans perceive their symptoms to be less severe [54], and believe that they have less access to health care [43] and that the health care system is less responsive to them once they do seek care [42]; thus, they may be less likely to see medical intervention as necessary or obtainable. It is important to recognize that perceptions of health, or ill health, are partially driven by cultural assumptions [55]. Therefore, racial differences in symptom reporting, or help seeking for symptoms, may be a function of culturally driven norms and expectations about health and illness [56]. In turn, help seeking may affect the likelihood of an individual being recruited into a research study.

It is also important to separate the relative contributions of race compared with other factors that may have an effect on research participation. These other factors might include socioeconomic status, educational level, understanding of the purpose of research, and perceptions of the costs and benefits associated with participating in a study.

One frequently cited barrier to research participation is the potential unpleasantness of interventions and their side effects [3,57-60]. Rosenberg et al [61] found that willingness to participate in clinical gerontologic research was inversely associated with the level of intrusiveness of the study; and that the greater the intrusiveness, the more relative influence a stipend had on eliciting participation. The intrusiveness of the research is inextricably tied to the type of research being conducted. For example, social scientists frequently employ survey research methodology, asking respondents questions about various issues. Some respondents may view talking with someone as far less intrusive than giving blood or undergoing a medical procedure, although the extent to which such activities form a continuum has not been fully established.

Rosenberg et al [61] also found that research that presented a new experience and an opportunity to learn was positively associated with willingness to participate. Conversely, a number of studies have shown that inadequate evidence of benefits from participation is a barrier to recruitment [3,60,62-64].

Educational level may be associated with a potential research participant's appreciation of the learning opportunities posed by research participation, as well as a better understanding of the purpose and process of research. Kressin et al [65] found a positive association between educational level and participation in VA-sponsored biomedical research. Other investigators have found similar results in civilian populations [3,21,66-68].

Beliefs about the efficacy of treatments and procedures also likely influence an individual's willingness to participate in studies about the efficacy of new therapies. James et al [69] found that African American men reported less confidence in the efficacy of antihypertensive drugs

than did African American women, white men, or white women. The continued existence of folk and alternative medicine among members of the African American community may also suggest a lack of confidence in conventional treatments [70]. Many Hispanic communities, including Puerto Ricans, also seek alternative medicine routes for care [71,72]. Further, doubts about the health care system's ability to equitably care for African Americans and Hispanic Americans may affect their perceptions about the efficacy of treatments and procedures offered to them, although this hypothesis needs to be tested.

It is also critical to identify the types of factors that individuals themselves believe may positively influence them to participate in biomedical research; for example, particular types of recruitment strategies, having study leaders who are members of the same racial group, and providing meaningful incentives [73]. One factor frequently cited by investigators for the low level of representation of minority and low-income groups in clinical trials has been the absence of insurance coverage for such participation (Baldwin, personal communication, 1996). This problem has been exacerbated recently because managed care has become an increasingly larger force in medical care insurance. Health-maintenance organizations have frequently defined clinical trials as providing “experimental treatments” for which they will not pay. A policy approved by the board of the American Association of Health Plans in 1997 marked the beginning of some progress in solving this problem [74].

Significance of the proposed TLP, as planned

An accurate understanding of the relative contributions of race and other factors that may be barriers or incentives to participation in biomedical research is crucial to the development of interventions and comprehensive recruitment strategies. The purpose of the TLP study is to accurately identify such barriers and incentives, and to assess their relative effects, in order to provide information that can be used to improve recruitment strategies for ongoing and future biomedical research. Findings from this study will provide the data or evidence for subsequent research to predict which people are likely to participate in clinical trials and other biomedical studies, and to suggest areas of concerns of nonparticipants, which may well include individuals who may be at highest risk for disease, that must be addressed in order to ensure that participant samples are reflective of the diversity of the nation's population.

Therefore, the primary aims of the TLP, as a study within the NMORHC, were to (1) determine whether there is a greater reluctance to participate in biomedical studies among minorities than among whites, and, if so, to explore those sociodemographic and psychosocial factors that might account for that observed difference; and (2) identify factors that may positively influence individuals to participate in biomedical studies.

The overall goals of this study were to address and understand a range of issues related to the recruitment of African Americans and other minorities into biomedical research studies. Attainment of this goal is critical in order to ensure that the findings from biomedical studies provide health data on the diverse populations of the United States and to provide empirical suggestions for interventional and other clinical studies on enlisting minorities into biomedical studies, including clinical trials.

Summer pilot studies to develop the TLP Questionnaire (1994–1998)

The TLP Questionnaire was developed within a research project of the NMOHRC. The TLP Questionnaire addressed a range of issues related to the recruitment of minorities into biomedical studies. Specifically, the goal of the TLP Questionnaire was to focus on whether minorities are more reluctant to participate in biomedical research studies and, if so, why.

The TLP Questionnaire was initially developed via a series of pilot studies conducted between 1994 and 1998. These pilot studies were typically summer research studies in which the faculty research team involved students from “Historically Black Colleges and Universities” and dental schools. Specifically, this series of pilot studies of the TLP were summer research projects led by Drs. Katz, Kegeles, Kressin, and Green, who were assisted each year by summer research interns from Spelman College, Morehouse College, Oakwood College, and local regional colleges (eg, Vassar College and Connecticut State University); and dental students from the University of Connecticut Health Center, the UMDNJ Dental School, New York University College of Dentistry, and the University of Puerto Rico School of Dentistry. On one occasion, a gifted high school student participated in one of these summer pilot studies. Pilot study I, conducted in the summer of 1994, utilized focus group research techniques under the guidance of Dr. Shedlin and Mr. Shulman from Sociomedical Resource Associates to identify the full range of issues that should be considered in developing a questionnaire on this topic; whereas pilot study II, conducted in the summer of 1995, utilized the information from the previous summer's findings and developed the first version of the TLP Questionnaire, which was a 78-item questionnaire.

Pilot study III, conducted in the summer of 1996, had the primary goal of field testing the TLP Questionnaire to permit its final refinement. Pilot study III consisted of two components. First, the TLP Questionnaire was formatted so that it could be administered in a telephone interview format and in a face-to-face interview. Second, the TLP Questionnaire, reduced to a 47-item instrument at this point, was given to four targeted convenience samples of 30 subjects each (African Americans, Jamaican Americans, Hispanic Americans, and non-Hispanic whites) for the primary purpose of determining individual reactions to the questionnaire itself, with a secondary purpose of providing preliminary data on response patterns to the questionnaire.

The findings from the three pilot studies were presented at the 1997 International Association for Dental Research Meeting and were published in the proceedings of that annual meeting [75]. During the summers of 1997 and 1998, pilot studies IV and V were conducted, which provided the administrative evaluation and field testing of the TLP Questionnaire in its final form, a 60-item questionnaire. Field testing of the final version of the TLP Questionnaire provided strong evidence that the instrument was fully understandable and did not exceed any subject's educational/attention/interest span.

TLP Questionnaire development at the Tuskegee workshop in January 1996

On January 18 and 19, 1996 a workshop was held at Tuskegee University on “Enhancing Minority Participation in Research and Other Programs Sponsored by the United States Department of Health and Human Services.” The primary goal of the workshop was to develop a strategy for an apology from the United States government to the African American community for the USPHS–Tuskegee syphilis study. This workshop was sponsored by the Minority Health Professions Foundation, funded by the Centers for Disease Control and Prevention (CDC) and the Office of the Assistant Secretary for Health of the Department of Health and Human Services, and organized by the NMOHRC under the joint guidance of Dr. James Ferguson (then dean of Tuskegee University College of Veterinary Medicine and president of the Minority Health Professions Foundation), Dr. Rueben Warren (then CDC's Associate Director for Minority Health), and Dr. Ralph Katz (Director of NMOHRC).

The workshop had two purposes: (1) to develop a strategy for an apology from the United States President, and (2) to have the national panel of 22 experts review and critique the TLP Questionnaire. The panel of experts at the workshop was composed of experts on the history and bioethical aspects of the USPHS–Tuskegee syphilis study and on issues of minority health. Members of the committee reviewed the 78-item questionnaire and provided many suggestions

for revision. Based on these suggestions, faculty working on this project within NMOHRC reduced and refined this interview instrument to a 47-item questionnaire that was subsequently field tested in pilot study III in the summer of 1996. In addition to Dr. Katz, two other member of the TLP research team—Drs. Kegeles and Green—were both participants at the workshop.

The unanticipated societal benefits: a presidential apology and a National Bioethics Center

A subset of the participants at this workshop at Tuskegee University formed the Tuskegee Syphilis Study Legacy (TSSL) Committee, chaired by Dr. Vanessa Gamble, associate professor of History of Medicine for University of Wisconsin and co-chaired by Dr. John Fletcher, Director of the Center for Bioethics, University of Virginia. The membership included Dr. Jim Jones (the author of *Bad Blood*), Dr. Ferguson, Dr. Katz, and Dr. Green. The goal of the TSSL Committee was to ensure that, subsequent to the workshop, the proposed apology document would be presented to the highest levels of government and to key community leaders.

The culmination of the committee's activity occurred a year and a half later on May 16, 1997 when President Clinton issued an apology to the survivors of the USPHS–Tuskegee study and the African American communities of the United States for the USPHS–Tuskegee syphilis study. Drs. Katz and Green were invited to the White House ceremony at which the apology was offered.

The unanticipated societal benefits of the presidential apology included far-reaching outcomes to the African American community for research abuse by the federal government and the establishment of a government-mandated National Center for Bioethics in Research and Health Care at Tuskegee University. When the NIDCR took a leadership stance at the NIH to address minority health issues by being among the first to establish a research agenda and functioning program to address issues of minority health via the RRCMOH, the NIDCR set in motion forces with societal impact that went well beyond whatever scientific goals it envisioned at that time. By reaching beyond strict scientific goals to include a societal component within its scientific agenda (as well articulated in the Request for Applications released in 1991 announcing the competition for these centers) NIDCR's leadership was, in fact—unexpectedly—critical to the occurrence of the presidential apology and the establishment of the National Center for Bioethics in Research and Health Care at Tuskegee University.

When the United States government went into a major budget crisis in the fall of 1995, it literally shut down for several weeks because Congress failed to pass a federal budget extension bill. It was during those specific weeks that the NMOHRC, as established by the NIDCR, was able to play a critical role in ensuring that the pivotal workshop at Tuskegee University, scheduled for January 1996, did not fall apart. With CDC staff in a suspended state, both the director of NIDCR's NMOHRC and the grant and data manager for the NMOHRC (Mr. Rene Lopez) worked nearly exclusively for several weeks to ensure that the array of potential attendees was finalized to achieve a final invitee list that was balanced to ensure appropriate federal government representatives, key academic leaders on the topic, and key health officials from the Tuskegee area and broader Alabama community. Further, these individuals from the NMOHRC then assumed responsibility to ensure that the identified attendees were—in point of fact—formally invited (envelope addressing and stuffing activities) to the meeting. Furthermore, these same two individuals made all arrangements for the workshop, and handled all participant correspondence related to the conference during that several-week period when the federal governmental was shut-down. The end result: a completely unanticipated role of an NIDCR creation in historical events that had significant societal impact.

The Huntsville Study: a “major” pilot study of all methodologic elements

In the summer of 1998, the TLP Questionnaire was administered to 100 African Americans and 100 non-Hispanic whites in the city of Huntsville, Alabama via a Random-Digit Dial (RDD) telephone survey conducted by the University of Alabama Survey Research Unit. The TLP Questionnaire again proved to be fully understandable to subjects and did not exceed participants' educational/attention/interest spans. The findings from this survey were presented by the principal investigator of this pilot study at the 1999 meeting of the American Public Health Association in Chicago. The Huntsville study indicated that both the TLP Questionnaire and the methodologic elements of the research design worked well. At this time, Dr. Sherman James—a psychologist and professor in the Department of Epidemiology at the University of Michigan, who had just left his position as associate dean for the School of Public Health at the University of Michigan—joined the multidisciplinary research team of the TLP.

Additional pilot summer studies: preparation for targeting Hispanic American populations

In the summers of 1999 and 2000, pilot studies VI and VII were conducted with the goal of producing a Puerto Rican Spanish version of the TLP Questionnaire. In 1999, two dental students from the University of Puerto Rico School of Dentistry worked at the University of Connecticut under the supervision of Dr. Katz. They each separately translated the TLP Questionnaire into Puerto Rican Spanish and then resolved the differences between their two translations in discussions with Dr. Katz, to ensure that the intended meaning of the original TLP Questionnaire wording was preserved. The two dental students completed this abbreviated pilot study by administering the Puerto Rican Spanish version to staff and clients at the Hispanic Health Council of Hartford, Connecticut, which led to minor modifications of the translation.

In preparation for the use of the Spanish version of the TLP Questionnaire in a pilot study for the summer of 2000, Dr. Katz visited the University of Puerto Rico School of Dentistry several times during the 1999–2000 academic year to initiate a collaboration with Dr. Cristina Claudio, a faculty member at the University of Puerto Rico School of Dentistry, on pilot study VII. This pilot study was designed to test the Spanish version of the TLP Questionnaire for use in a major study that would investigate the effect of acculturation on Hispanics into US life regarding willingness to participate in biomedical research studies by comparing Puerto Rican Hispanics who had lived in New York City for at least 5 years with Puerto Rican Hispanics who had lived in San Juan all of their lives. A total of over 140 interviews were conducted in New York City and San Juan by dental students from the University of Puerto Rico, which provided valuable information for making final modifications to the TLP Questionnaire.

The 3 City TLP Study: specific aims and preliminary findings

The specific aims of the 3 City TLP Study were to (1) determine whether (and if so, the extent to which) African Americans indicated greater reluctance to participate in biomedical studies than did non-Hispanic whites, Jamaican Americans, and Puerto Rican Americans; (2) determine the influence of sociodemographic factors, psychosocial factors, specific study circumstance factors, and knowledge and perceptions of medical historical events factors on the comparative willingness of African American, non-Hispanic whites, Jamaican Americans, and Puerto Rican Americans to participate as study subjects; and (3) to identify factors that may positively influence African Americans, non-Hispanic whites, Jamaican Americans, and Puerto Rican Americans to participate in biomedical studies.

The TLP Questionnaire, a 60-item instrument, was administered via an RDD telephone interview by the University of Alabama at Birmingham Survey Research Unit to 840 adult

African Americans and whites in three city/county areas—Birmingham/Jefferson County, Alabama; Hartford/Hartford County, Connecticut; and Tuskegee/Macon County, Alabama—in 1999 and 2000. Preliminary analyses on the comparison of African Americans versus non-Hispanic whites in the 3 City Study were conducted. The response rates were 70%, 65%, and 49% for Birmingham, Tuskegee, and Hartford, respectively.

A lower percentage of African Americans (21%) reported that they were either somewhat or very likely to participate as biomedical research subjects than did whites (29%, $P < 0.0001$). In response to seven questions on "who was conducting the study," African Americans indicated that they were less likely to participate than were whites on four specific questions and more likely to participate on only one question ($P < 0.006$ for each). In response to nine questions on "what they would be asked to do in a study," African Americans indicated that they were less likely to participate than were whites on only two specific questions ($P < 0.001$ for each), more likely to participate on two questions ($P < 0.001$), and equally or near equally likely to participate on five prompts. Logistic regression analysis revealed that African Americans were less likely to participate as research subjects than were non-Hispanic whites (odds ratio [OR] = 0.696, $P < 0.05$) after adjusting for age, gender, education, and income. Similarly adjusted logistic regression analyses regarding the influence of "who was running the study" and "what they would be asked to do in a study," revealed that African Americans were less likely to participate based on the "who" (OR = 0.71, $P = 0.068$) but not the "what" (OR = 1.05, $P = 0.78$). The findings from the descriptive and the logistic regression analyses in this study showed that African Americans self-reported a lower willingness to participate in biomedical studies than did non-Hispanic whites, and suggested that African American subjects were more negatively influenced by the factor of who was running the study but not by the factor of what they might have to do as study subjects. The descriptive results of these bivariate preliminary analyses were presented at the American College of Epidemiology Meeting in Atlanta in September 2000 [76].

The logistic regression analyses of these preliminary analyses were submitted as an abstract for the American Association for Dental Research Meeting in Chicago in 2001. The findings from this logistic regression analysis were in total agreement with the above-mentioned bivariate findings on African Americans versus non-Hispanic whites, with regard to direction and magnitude of relationships.

The 4 City TLP Study: the San Antonio TLP component added

The 3 City TLP Study (Birmingham, Alabama; Tuskegee, Alabama; and Hartford, Connecticut) was expanded to include a sample of subjects in San Antonio, Texas. Given that the Hartford, Connecticut sample included a sample of Puerto Rican Americans as a Hispanic group, San Antonio was added to provide a sample of another Hispanic-American group: Mexican Americans. The TLP Questionnaire (English language version only) was again administered via an RDD telephone interview by the University of Alabama at Birmingham Survey Research Unit to a target of 100 Mexican American participants and a comparison group of 100 non-Hispanic whites in San Antonio. These data were added to the data from Birmingham, Tuskegee, and Hartford to form the 4 City TLP Study. This 4 City TLP Study has a total of over 1200 research participants and will allow for a direct comparison of African Americans versus Hispanics versus whites across the four cities, and subcomparisons within ethnic groups (eg, African Americans versus Jamaican Americans and Puerto Ricans versus Mexican Americans). These data for the 4 City TLP study are currently being analyzed.

The "legacy" of the TLP: the next generation of related studies

The NIDCR, having established itself as an early leader on health disparities, has continued its institutional commitment to supporting this line of investigation by funding five Centers

for Research to Reduce Oral Health Disparities in 2001. One of the funded "disparities centers," the New York University Oral Cancer Research for Adolescent and Adult Health Promotion (RAAHP) Center, is conducting a major study directly derived from the 4 City TLP Study. The two questionnaires that are the primary research instruments in this new study (the Cancer Screening Questionnaire and the Research Subject Questionnaire) are, in fact, shortened and slightly modified versions of the TLP Questionnaire. Both questionnaires address the issue of differential participation by minorities in health activities: one focuses on willingness to participate and factors that affect participation in cancer screenings, and the other is being used to continue to gather data on the reasons why individuals do or do not volunteer to be research participants. This study was initiated in the fall of 2001, with the anticipated completion date for the field data collection phase being the spring of 2004.

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